

In support of the Request For Continuing Examination and the substantive Response to the most recently received (final) Official Action mailed April 11<sup>th</sup>, 2003 submitted herewith, applicants now formally reply to the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures and hereby amend the Specification of the above-identified application pursuant to 37 C.F.R. 121. Such amendment is being made by submission of replacement paragraphs for the Specification, in clean copy form, for the changes listed below. A marked-up copy of these replacement amended paragraphs is also provided as a separate document.

In the Specification:

Amend the Specification text appearing at:

Page 29, lines 19-20.

In addition, pursuant to and in compliance with the requirements of 37 C.F.R. 1.821-1.825, applicants also enclose herewith a third paper form copy of the "Sequence Listing" containing disclosures of nucleotide sequences and/or amino acid sequences. Applicants respectfully request and direct that the enclosed third paper form copy of the "Sequence Listing" containing disclosures of nucleotide sequences and/or amino acid

sequences be formally entered into and be made officially of record for the Specification of the above-identified application.

Applicants' undersigned attorney also declares and verifies that this amendment and requested formal entry of the "Sequence Listing" in paper form copy is proper and correct in all respects; and that the enclosed "Sequence Listing" in paper copy form is completely supported by the descriptive content and enabling disclosure of the Specification text originally filed September 2, 1998 as USSN 09/145,916.

Furthermore, applicants' undersigned attorney also declares and verifies that the enclosed "Sequence Listing" submitted in paper form copy does not contain or include any New Matter; and that a third submission of a computer readable form (CRF) copy of the "Sequence Listing" is also provided, the third computer readable form (CRF) copy being identical in substantive content to the enclosed third paper form copy.

Accordingly, this third paper form copy "Sequence Listing" is to be formally entered into and made part of the Specification; and the formally entered third paper form copy "Sequence Listings" shall now constitute part of the Specification during the substantive prosecution of this application.

Respectfully submitted,

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### 1 C. The Cytoplasmic Domain Coding For The Syndecan-4 Peptide

2  
3 The third requisite cytoplasmic domain must code for the amino acid  
4 residue structure representative of the syndecan-4 core protein. As shown  
5 experimentally by the data presented hereinafter, only the syndecan-4 cytoplasmic  
6 region and peptide structure allows for functional stimulation of angiogenesis in-  
7 situ. For this reason, it is essential and required in each embodiment of the  
8 present invention that the third DNA sequence coding for the cytoplasmic domain  
9 in the expressed proteoglycan entity in a transfected endothelial cell be  
10 representative of and analytically identifiable as the syndecan-4 amino acid residue  
11 structure. A representative recitation of the DNA constituting the cytoplasmic  
12 domain of the syndecan-4 molecule is presented by Fig. 13 herein.

13 It will be noted and recognized that very little variability and substitution  
14 within the specific DNA base sequencing of the cytoplasmic domain of the  
15 syndecan-4 molecule is permitted. While some changes are expected, be they  
16 point mutations, block substitutions and the like, the expected or envisioned degree  
17 of variability which might be present or permitted for the cytoplasmic domain  
18 DNA is believed to be quite limited.

19 As representative examples: The last four amino acids (EFYA) [SEQ ID  
20 NO:25] cannot be changed or modified. Similarly, regarding the Serine residue at  
21 position 181: a mutation to an Alanine residue potentiates activation; while a  
22 mutation to Glutamate inhibits cell growth in a dominant fashion (dominant-negative  
23 mutation). Finally, the LGKKPIYKK sequences [SEQ ID NO:24] probably cannot be  
24 altered at all.